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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/688,254	10/13/2000	Harry M. Meade	GTC-43	9900
23628	7590	11/27/2007		
WOLF GREENFIELD & SACKS, P.C. 600 ATLANTIC AVENUE BOSTON, MA 02210-2206			EXAMINER QIAN, CELINE X	
			ART UNIT 1636	PAPER NUMBER
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

Application No.

09/688,254

Applicant(s)

MEADE ET AL.

Examiner

Celine X. Qian Ph.D.

Art Unit

1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 30 August 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 21-23 and 43-57 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 21-23 and 43-57 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on 13 November 2002 is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 0807, 1007
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

Claims 21-23, 43-57 are pending in the application.

This Office Action is in response to the Amendment filed on 8/30/07.

#### ***Response to Amendment***

Claims 21-23, 43-49, 51-57 are rejected under 35 U.S.C.103 (a) for reasons set forth of the record mailed on 2/28/07 and further discussed below.

Claim 50 is rejected under 35 U.S.C.112 1<sup>st</sup> paragraph for reason given below.

#### ***Response to Arguments***

#### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 21-23, 43-49, 51-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cheng et al. (5,981,714), in view of Radford et al. (5,955,270), Wagner et al. (6,329,209), Meade et al. (5,750,172), and Nuijens et al. (1997, JBC, Vol.272, No.13, pp.8802-8807). This rejection is re-written to address the claim amendment and newly added claims.

Cheng et al. teach a method of purifying a target polypeptide by using antibody which binds to a matrix. Cheng et al. also teach that the standard method for such purification consists preparation of antibody-matrix, binding an antigen to the antibody-matrix, removing contaminants by washing, and elution of the antigen (see col. 7 line 56 through line 12, col. 8). However, Cheng et al. does not teach that the antibody is made transgenically. Cheng et al. do

not teach that the target polypeptide is an antibody. Cheng et al. do not teach that the target polypeptide is a receptor. Cheng et al. do not teach that the antibody used to purify the polypeptide having CBD. Cheng et al. do not teach that the polypeptide is produced in an inactive form or inactivated by binding of a multivalent polypeptide.

Radford et al. teach that by adding the cellulose binding domain to an expression construct makes it easier for the subsequent purification (col. 2 line 59 through col.3 lines 13). Radford et al. further teach a method of purifying cellobiohydrolase-1 comprising the cellulose-binding domain can be used to bind to a cellulose matrix and washing off other components, thereby purifying said enzyme.

Wagner et al. teach that a method of capturing proteins to an array chip by using capturing agents that are attached to the chip (col.3). Wagner et al. also teach that the capturing agents can bind a protein to itself in a specific manner. They include antibodies, wherein the binding partner is antigen, and receptors, wherein their binding partner is ligand (see col.4, lines 48-67).

Nuijens et al. teach the expression and characterization of the recombinant human lactoferrin secreted in milk of transgenic mice. Nuijens et al. teach that the transgenically produced lactoferrin is very similar to the natural lactoferrin, and exerts same anti-bacterial and anti-inflammatory activities in vivo.

Meade et al. teach the production of a number of recombinant proteins including TPA, urokinase, growth hormones and immunoglobulins in the milk of transgenic non-human mammal (see col.3, 3<sup>rd</sup> paragraph, and Examples 1-3).

Based on the combination of teaching of Cheng et al. (5,981,714), and Nuijens et al. (1997, JBC, Vol.272, No.13, pp.8802-8807), it would have been obvious to one of ordinary skill in the art to develop a method of purifying target polypeptide either from milk of a transgenic mammal or other mixtures by contacting the target polypeptide with a transgenically produced multivalent binding polypeptide, (for example, the antibody that is capable of binding to a matrix taught by Cheng et al.) having a first bindable epitope which binds the target polypeptide (for example, the antigen taught by Cheng et al.) and a second bindable epitope which binds a matrix, and subsequent elution of the polypeptide from the matrix. The ordinary artisan would have been motivated to do so because a transgenically produced polypeptide is structurally same as the natural occurring polypeptide as demonstrated by Nuijen et al. Further, Meade et al. teach the generation of recombinant immunoglobulins in the milk of the transgenic non-human mammal. Regardless whether the multivalent binding polypeptide is produced in the milk of the same transgenic mammal as the target polypeptide or in the milk in a second transgenic mammal, it can be used to purify the target polypeptide. The teaching of Cheng et al. does not specially indicate that the antibody needs to be separately purified before use. At the time of filing, the skill of art in producing recombinant protein in milk of transgenic mammal is high. Absent evidence to the contrary, one of ordinary skill in the art would have reasonable expectation of success to develop such a purification method using the multivalent polypeptide that is produced by a transgenic mammal, either in the same transgenic mammal that produces the target polypeptide or in a different transgenic mammal. Therefore, the invention would have been *prima facie* obvious to one of ordinary skill of art at the time the invention was made.

It would also have been obvious to one of ordinary skill of art to use CBD as the second binding moiety of the multivalent polypeptide based on the teaching of Cheng et al. (5,981,714), Radford et al. (5,955,270), and Nuijens et al. (1997, JBC, Vol.272, No.13, pp.8802-8807). The ordinary artisan would have been motivated to do so because Radford et al. teach that CBD binds to cellulose matrix and makes it easier to purify proteins comprising this domain. Since the nucleic acid sequence encoding those binding domains are known, attaching them to a polypeptide would have been routine experimentation at the time of filing. Absent evidence from the contrary, the ordinary skill of art would have reasonable expectation of success to produce a multivalent polypeptide with CBD domain as second binding moiety transgenically and use it to purify a target polypeptide such as IgGs. Therefore, the invention would have been *prima facie* obvious to one of ordinary skill of art at the time the invention was made.

It would also have been obvious to one of ordinary skill of art to use a receptor as the first binding moiety when the target polypeptide is a ligand or vice versa based on the teaching of Cheng et al. (5,981,714), Wagner et al. (6,329,209), and Nuijens et al. (1997, JBC, Vol.272, No.13, pp.8802-8807). One of ordinary skill of art would have been motivated to do so because Wagner et al. teach that receptor-ligand and antigen-antibody interaction is specific for protein capturing agent to bind to the ligand in a biological sample. Many receptor and ligand have been cloned and characterized at the time of filing. One ordinary skill of art would have plenty of information to choose receptor when a ligand needs to be purified and vice versa. Absent evidence from the contrary, one of ordinary skill of art would have reasonable expectation to transgenically produce a multivalent polypeptide with a binding moiety from either a ligand or a

receptor. Therefore, the invention would have been *prima facie* obvious to one of ordinary skill of art at the time the invention was made.

It would have been obvious to one of ordinary skill in the art at the time of filing to produce the target polypeptide in either activated or inactivated form depending on the nature of the target polypeptide being produced. Meade et al. and Nuijens et al. have already demonstrated that various protein may be produced in the milk of the transgenic animal which reflects that the state of art of producing polypeptide in milk of a transgenic animal is feasible. Further, it is known that certain proteins such as caseins or lactoglobulin exists a preprotein form which needs to be activated by protease cleavage. As such, producing a polypeptide in an inactivated form and later activated by protease is obvious because it is a known technique that is recognized as part of the ordinary capabilities of one ordinary skill in the art. Therefore, , the invention would have been *prima facie* obvious to one of ordinary skill of art at the time the invention was made.

Applicants argue that the above rejection does not establish the obviousness of the amended claims because none of the references alone or in combination teach or suggest the step of co-expression of both a target polypeptide and a multivalent binding polypeptide in a product of a non-human transgenic animal. In response to applicant's argument, Applicants are reminded that KSR forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness (See Board decision Ex parte Smith). Therefore, this rejection is maintained and applies to newly added claims for reasons discussed above.

***New Grounds of Rejection Necessitated by Amendment***

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 50 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 50 is drawn to a method of obtaining a target polypeptide having a bindable epitope from a product by co-expressing the target polypeptide and a multivalent binding polypeptide in a product of a non-human animal, wherein the multivalent binding polypeptide has a first binding moiety that binds the target polypeptide, and a second binding moiety that binds a matrix, and said multivalent binding polypeptide removes the bindable epitope from the target polypeptide. However, the specification does not describe such a multivalent polypeptide. The specification, on page 3, 7, 8, describes that the bindable epitope is removed by a second multivalent polypeptide that binds to a different matrix than the first multivalent polypeptide. It is apparent that there are two multivalent binding polypeptide, which one is for binding the target polypeptide and a matrix, wherein the second one is to remove the epitope and binding to a different matrix. Therefore, the newly added claim 50 contains new matter.

***Conclusion***

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X. Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joe Woitach Ph.D. can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Celine X Qian Ph.D.  
Examiner  
Art Unit 1636

CELINE QIAN, PH.D.  
PRIMARY EXAMINER

